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Ischemic Heart Disease

Precarious Coronary Lesions and Prognosis

ALBERT A. KATTUS, MD; ANNE H. COULSON, *and* MADELINE KARRASCH, DDS, *Los Angeles*

Coronary arteriograms in 113 patients whose cases were followed for 2 to 12 years were analyzed in an attempt to discover why in some patients with angina pectoris there are long stable clinical courses and in others the courses proceed rapidly to death. It was found that patients with completed coronary occlusions, usually with distal portions reconstituted by collateral, had favorable prognoses with prolonged longevity. Patients with multiple high grade narrowings of the coronary arteries, on the other hand, had poor prognoses with high attrition rates. The more stenotic lesions present in the coronary arteries, the higher the attrition rates. Completed coronary occlusions, therefore, have been classified as nonprecarious while local coronary stenoses greater than 50 percent of the lumen diameter have been classified as degrees of precariousness according to the number of lesions present.

When compared with classification by number of diseased vessels and by arteriographic score of Friesinger, the nonprecarious cases had better prognoses than the precarious.

IN SOME PATIENTS with angina pectoris of effort the clinical courses are remarkably prolonged and stable, uncomplicated by coronary events; in others similar clinical characteristics seem to be present but the courses proceed rapidly to death. In the hope of finding an explanation for the wide disparity in the clinical courses among patients with myocardial ischemia, a study was undertaken in which an attempt was made to trace the patients in whom coronary angiography was done in the years between 1960, when we first began to use this technique in our institution, and the year 1971, when bypass graft operations became commonplace. As review of the patient records proceeded and as the old angiograms were studied, it became evident that patients who had long uncomplicated survival despite anginal symptoms and evidence of myocardial ischemia shown on exercise electrocardiograms had coronary arteries with one or more complete obstructions compensated by collateral circulation from unobstructed arterial segments. In those patients whose clinical courses proceeded to early coronary death, angiograms showed high grade narrowings in major coronary arteries with antegrade flow through the stenotic segments.

These observations led to the concept that a completely occluded coronary artery is inherently stable because it cannot worsen and is, therefore, nonthreatening. An occluded artery has the potential for improvement if its collateral flow were

From Division of Cardiology, Department of Medicine, UCLA School of Medicine and Division of Epidemiology, UCLA School of Public Health, Los Angeles. Ms. Coulson is senior statistician in the Division of Epidemiology.

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Reprint requests to: Albert A. Kattus, MD, 501 East Hardy St., Suite 404, Inglewood, CA 90307.

ABBREVIATIONS USED IN TEXT
CFX=circumflex coronary artery
LAD=left anterior descending coronary artery
Rt=right coronary artery

to increase or if recanalization of the occluded segment were to occur. Complete coronary occlusion, therefore, might be considered a nonprecarious lesion because it is stable and predictable. Tight stenoses of coronary arteries, on the other hand, are inherently unstable because they are unpredictable. They are likely to progress at some time to complete closure but one cannot predict how or when. If the closure is gradual then collateral channels may have time to develop a compensating blood supply. If, however, closure is abrupt, a coronary event is likely to occur in the form of myocardial infarction or sudden death. Consequently, local stenotic lesions of coronary arteries have come to be regarded by us as precarious, and experience has indicated that the more such lesions there are the higher is the degree of precariousness.

The most commonly used method of grading the severity of coronary obstructive lesions and relating this to prognosis consists of counting the number of major coronary arterial trunks that harbor obstructive lesions (usually 50 percent or more narrowing of the lumen). Cases are classified, therefore, as having one-vessel, two-vessel or three-vessel coronary obstructive disease.[1-3] Actuarial survival curves have been published from several centers showing that one-vessel disease carries a low mortality risk, two-vessel disease a higher risk and three-vessel disease a very high mortality. In this method there is no discrimination between total occlusion and various degrees of stenosis.

Friesinger and his associates[4] have attempted to develop a more discriminating grading system which they have called the coronary angiographic score. A point system is used to rate the severity of the obstructive lesions with five points for total occlusion, ratings from one to four points for varying degrees of partial obstruction and zero for no narrowing. The maximal angiographic score is 15, indicating complete obstruction in all three major coronary arteries. In this system a complete occlusion (regarded by us as nonprecarious) is given a higher score than a tight stenosis (regarded by us as having a degree of precariousness).

Friesinger has presented survival curves showing low mortality for scores 1 to 4, intermediate mortality for scores 5 to 9 and very high mortality for scores 10 to 15.

We were able to trace 113 patients in whom reliable follow-up data could be combined with angiograms of interpretable quality. The angiograms in the cases were reread and classified according to precariousness by the method to be described subsequently. They were also classified according to the number of obstructed vessels and according to the angiographic score. To show the prognosis according to these three methods of classification, actuarial survival curves were constructed.

Patients and Methods

Hospital records were reviewed on 165 patients in whom coronary angiography was done for the study of ischemic heart disease. Patients in whom coronary arteries were visualized incidental to hemodynamic studies of congenital, valvular or myocardiopathy disease were not included. Excluded from the study were nine patients who had large ventricular aneurysms or ventricles so badly damaged that ejection fractions were below 40 percent. Small areas of akinesis or dyskinesis at the sites of healed infarcts were not considered disqualifying. Four patients were excluded because bypass graft operations were carried out less than a year after angiograms were done. Other causes for exclusion were lost angiograms (11 cases), angiograms of uninterpretable quality (7 cases), lost charts or missing information (3 cases), inability to trace patient (18 cases).

Full information was available on 105 men and 8 women ranging in age from 30 to 72 years, with a mean of 50 years. Reason for study in all but nine cases was the presence of chest pain resembling angina pectoris. In two there were ischemic responses on treadmill exercise testing without anginal pain and in seven there was rest angina with good exercise tolerance (Prinzmetal variant angina).[5] Three coronary angiograms in the series were done by the aortic root flushing technique in 1960. Subsequently, angiography and ventriculography were done by the Sones[6] or Judkins[7] technique.

The cineangiograms were all read independently by the senior author and compared with the original radiologic reading. When differences of interpretation arose the disagreements were adjudicated with Julius Grollman, MD, Chief of

Cardiologic Radiology, University of California, Los Angeles, so that all interpretations represented a consensus among at least two readers. Patient follow-up was obtained by personal contact, communication with private physicians, mail questionnaire or telephone communication with the patients.

Determining Degrees of Precariousness

Coronary arteries that were open throughout containing no narrowing greater than 50 percent were considered to have zero degree of precariousness. Also considered nonprecarious were coronary arteries or their primary branches which were totally occluded. This classification held whether or not the vessel was reconstituted by collateral circulation beyond the occlusion. Each stenotic lesion greater than 50 percent in the major coronary arteries or their primary branches was considered one degree of precariousness. A single artery can yield a precariousness greater than one since it may have multiple discrete stenoses. A precarious lesion in the left main coronary artery was given a rating of two degrees because both circumflex and anterior descending systems are jeopardized by such a lesion. A narrowing in a vessel for which another artery which could serve as the source for collateral supply has already been totally occluded is also given a double rating since the reduced availability of collateral supply increases the jeopardy.

Examples of Nonprecarious and Precarious Disease

The concept of the precarious and nonprecarious coronary lesions is best presented by reference to the following examples in which the method of rating according to degree of precariousness is illustrated. The examples also indicate the ratings according to the number of diseased vessels and according to Friesinger's angiographic score.

The prototype for the nonprecarious state is illustrated in Figure 1 which shows the coronary arteriographic findings in a man with nondisabling angina pectoris and pronounced ischemic electrocardiographic changes during treadmill exercise whose case had been followed for eight years of an uneventful clinical course. Study of the angiogram in this case as shown in the diagram discloses that there is complete occlusion of the anterior descending (LAD) and the circumflex (CFX) marginal coronary arteries, both of them reconstituted by retrograde flow from collateral channels fed from the unimpeded right coronary artery. The stable clinical course in this patient is believed to be due to the fact that the obstructive lesions are complete and, therefore, cannot worsen, but they could conceivably improve if collateral flow were to increase or if recanalization were to take place. The complete occlusion is taken to be a nonprecarious lesion because it appears to represent a stable state not likely to change abruptly. In this patient, therefore, there is no precariousness with two-vessel disease. The coronary arteriographic obstruction score of Friesinger is 7 (LAD-5, CFX-2).

The prototype of the precarious coronary circulation is illustrated in Figure 2. This shows coronary angiographic findings in a man with disabling angina who died suddenly one week after the angiogram. The anterior descending coronary artery has a proximal high grade stenosis and the right coronary artery (Rt) is com-

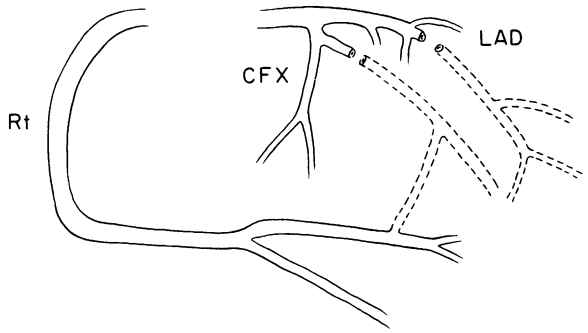

Figure 1.—Diagram of nonprecarious coronary circulation derived from study of selective cineangiograms. Dotted lines indicate vessels reconstituted by collateral flow distal to occlusion. Diagram represents a composite of left anterior oblique view of right coronary and right anterior oblique view of left system. Rt = right coronary, CFX = circumflex, LAD = left anterior descending, LAD and CFX marginal are completely occluded.

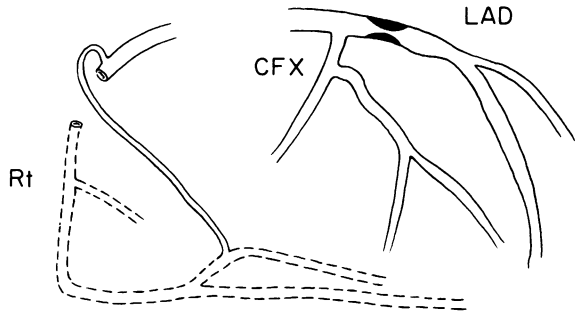

Figure 2.—Diagram of precarious coronary circulation. There is high grade stenosis in left anterior descending coronary artery (LAD) and complete occlusion of right coronary artery (Rt) with reconstitution via collateral channels. CFX = circumflex.

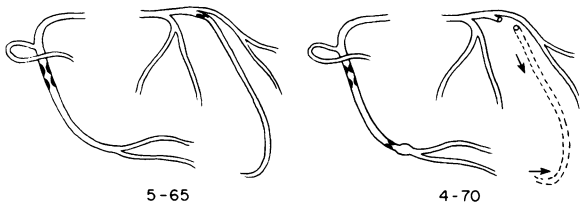

Figure 3.—Diagram of precarious coronary circulation on left. Repeat arteriogram five years later shows closure of one stenotic lesion which produced myocardial infarct. A new stenotic lesion had also appeared in the right coronary.

pletely occluded but filled by bridging collaterals. The pronounced narrowing in the anterior descending is taken to be highly precarious because it is likely to progress to complete occlusion and it cannot be predicted when this might happen or whether it will occur gradually or abruptly. Furthermore, the lesion carries double jeopardy to the anterior myocardium because its major possible source of collateral flow is already eliminated by total occlusion of the right. In this case there is two-vessel disease with two degrees of precariousness; coronary arteriographic score 8 (Rt-5, LAD-3).

In Figure 3 are illustrated two coronary angiograms taken five years apart on a 46-year-old man who was first disabled by angina, improved on an exercise training program and subsequently had a nonfatal myocardial infarction. The first angiogram made during severe angina disability showed two pronounced stenoses in the right coronary artery and one in the anterior descending coronary artery representing three degrees of precariousness, one for each local stenotic lesion. Four years after the first angiogram an anteroseptal myocardial infarction occurred without warning. In a subsequent repeat coronary angiogram it was shown that the anterior descending coronary artery had closed at the site of the previous local stenosis. The two right coronary stenoses previously seen remained unchanged, but a new stenosis had appeared in the distal right coronary with poststenotic dilatation beyond. In this man with two-vessel coronary disease there were four distinct points of coronary narrowing, one of which apparently closed abruptly to produce a coronary event. It is reasoned that any one of the four narrow points could have gone on to closure and there was no way to predict which one would do it or when. Hence, we rate this patient as having had four degrees of precariousness before the infarct. Coronary arteriographic score was 5 (Rt-3, LAD-2) on the first angiogram and 8 (Rt-4, LAD-4) on the second.

Data Handling

All coronary angiograms were rated by the three different systems described. Considering the day on which the angiogram was done as time zero, survival curves were constructed by age-adjusted actuarial methods.[8] Only the cases of patients who died from coronary causes are included in the attrition rates. There were 37 cardiac-related deaths in the series and 2 due to noncardiac causes. The deaths from cardiac causes are tabulated in Table 1. Nine of the deaths were related to surgical attempts at revascularization, six to bypass vein grafting, one to Vineberg in-

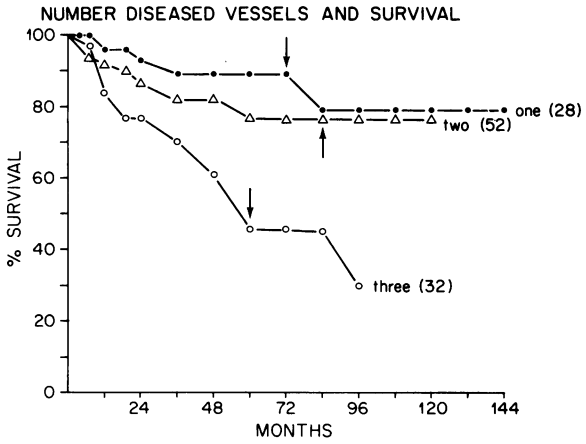

Figure 4.—Survival curves actuarially computed based on one-, two- and three-vessel coronary obstructive disease. Number of patients in each group in parentheses at right. Vertical arrows indicate the interval in months at which the number of subjects drops below ten.

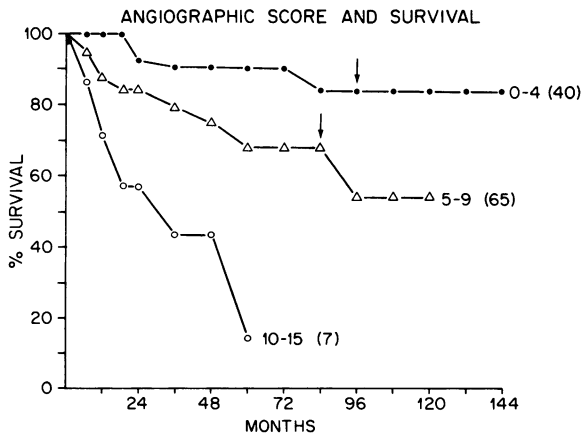

Figure 5.—Survival curves based on angiographic score. Number of patients in each group in parentheses at right. Vertical arrows indicate the interval at which the number of subjects drops below ten.

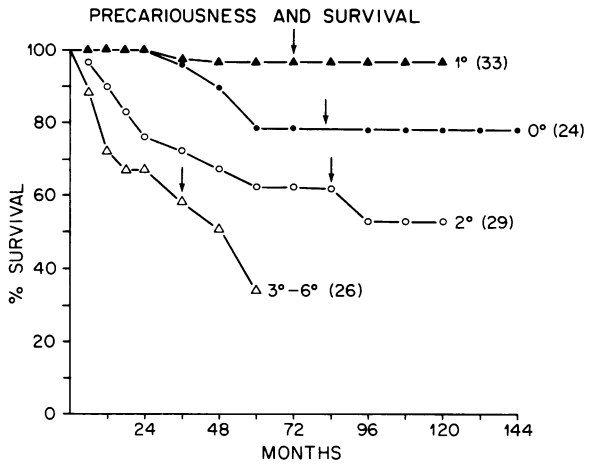

Figure 6.—Survival curves based on degrees of precariousness. Number of patients in each group in parentheses at right. Vertical arrows indicate the interval at which the number of subjects drops below ten.

ternal mammary implantation procedures and one to coronary endarterectomy. The interval between the initial catheterization and operation in these patients ranged from 12 to 103 months; the average was 40 months. Two deaths also occurred during heart catheterization and these are regarded as cardiac deaths and included in the survival curves. Deaths resulting from attempted coronary revascularization operations are not included as coronary deaths because presumably the patients would have survived longer if the operations had not been carried out. The cases of these patients and also those of patients lost to follow-up are treated as though the period of follow-up terminated when the patients were last known to be alive. The cases of six patients in whom revascularization operations were done successfully are also classified as though the period of follow-up ended on the day of the operation. The interval between initial catheterization and operation in these patients averaged 63.7 months with range from 27 to to 96 months.

In view of the limited size of the study population (a total of 113 patients), the survival curves shown should be interpreted in terms of the consistency of trends, and only cautiously in terms of the absolute shape of the curve. Axtell[9] indicates that survival rates are not acceptable where fewer than ten cases enter the interval alive, and should be interpreted with care where less than 50 cases enter the interval alive. The number of cases in each subgroup entering the study is shown in Figures 4 through 8. In Figures 4, 5 and 6 vertical arrows indicate the interval in months at which the number of subjects drops below ten for each classification group and subgroup included in the survival curves. A life table procedure for analyzing longitudinal studies described by Fleiss and co-workers[10] was used to test for the significance of the difference between two series of probabilities.

Results

Survival curves for the three different rating methods are shown in Figures 4, 5 and 6. Attrition rates for the classifications by number of diseased vessels and by the angiographic score are comparable to those published by others.[1-4] The attrition rates for the various degrees of precariousness follow expected trends for degrees 2

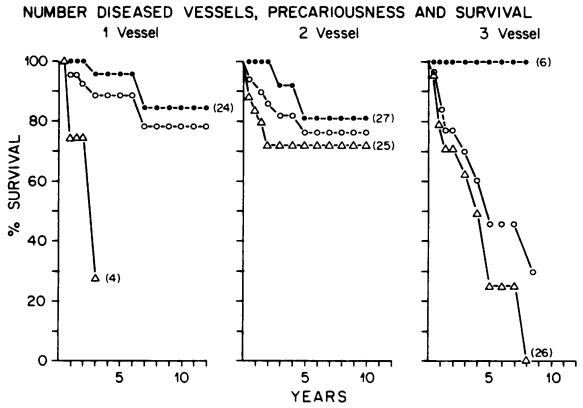

Figure 7.—Survival curves for patients with one-, two- and three-vessel obstructive disease. Open circles represent the whole group as seen in Figure 4. Closed circles are those with zero or one degree of precariousness. Triangles are those with two to six degrees of precariousness.

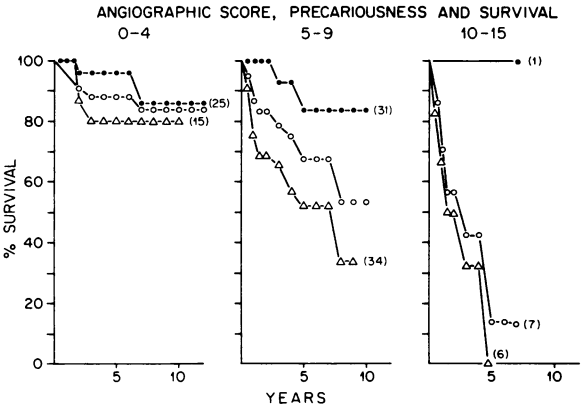

Figure 8.—Survival curves for patients classified by angiographic score. Open circles represent whole group as in Figure 5. Closed circles represent those with zero or one degree of precariousness. Triangles represent those with two to six degrees of precariousness.

and above. Unexpected is the observation that the one-degree precarious group fared better than the zero-degree group. However, this difference is not statistically significant. Therefore, the zero-degree and one-degree groups can be combined to constitute a single low-risk group. (Table 1)

Each group of patients classified by the number of diseased vessels and by the arteriographic score method may be subdivided into two populations, precarious and nonprecarious. Considering those with zero and one degree as nonprecarious and those with two to six degrees as precarious, each of the number of diseased vessel and arteriographic score classes has been subdivided into precarious and nonprecarious populations and survival curves plotted as in Figures 7 and 8. In each instance the precarious group has a higher mortality than the nonprecarious group. Of particular interest is the group of six nonprecarious patients with three-vessel coronary disease with no mortality over eight years of observation.

Despite the relatively small numbers, these differences in trend between the precarious and nonprecarious groups were significant over the first two-year period for one- and two-vessel disease ($p<.05$). In one-vessel disease no further evaluation was possible. Five- and ten-year trends for two-vessel disease were not significantly different. Trends for three-vessel disease were significant over the three-, five- and ten-year periods ($p<.05$, $<.01$ and $<.01$, respectively). In the three angiographic score groups the difference in trends was not significant in the low score group but was consistently significant ($p<.01$) in the intermediate group. In the high score group the numbers were too small to allow testing.

Discussion

The findings in this historical prospective study support the concept that the completed coronary closure is a nonprecarious obstructive lesion that is predictable and compatible with a long uncomplicated clinical course even though ischemic manifestations may be present. Local stenotic lesions, on the other hand, are found to be precarious because they are associated with high risk of mortality, and the more there are of such lesions the higher is the risk.

TABLE 1.—*Mortality and Degrees of Precariousness*

Degrees of Precariousness	*No. of Cases*	*Coronary Deaths*	*Mortality Percent*	*Manner of Death*			
				Sudden Death	*Myocardial Infarct*	*Operative*	*Cath*
0	24	6	25	3	1	2 BP	..
1	33	2	6	..	..	1 END	..
						1 VB	
Low precarious (0-1)	57	8	14				
2	29	12	41	4	7	1 BP	..
3	16	8	50	4	1	2 BP	1
4-6	11	9	82	3	3	2 BP	1
High precarious (2-6)	56	29	52				
Totals	113	37	32.7	14	12	9	2

BP = bypass vein graft END = coronary endarterectomy VB = Vineberg implant

TABLE 2.—*History of Coronary Artery Lesions Seen in Sequential Coronary Angiograms—25 Cases*

	Right Coronary	*Circumflex*	*Anterior Descending*	*Total*
Complete occlusions stable	11	5	6	22
Average patient months*	35	44	32	..
Stable stenosis	5	6	10	21
Average patient months	44	42	33	..
Progressive narrowing	17	7	8	32
Average patient months	38	48	44	..
New disease	8	1	4	13
Preexisting stenosis	9	6	4	19
Total closure	5	5	2	12
Number with myocardial infarction	1	0	1	2

*Average time per patient between first and second angiogram.

The method of assigning degrees of precariousness has purposely been kept simple in order to test its validity. The only weighting of the precarious lesion has been to double its value in left main lesions and in cases in which a possible source of collateralization has already been obliterated. This fails to take into consideration the higher risk of anterior descending lesions which have been shown to have increased mortality.[11,12] The very high risk of the left main coronary lesion[13] is confirmed by our finding that eight of 14 patients with that lesion had died, with an average survival time of 15 months. Of six surviving patients, revascularization procedures were done successfully in three.

It was not possible to trace the distribution of standard coronary risk factors such as blood cholesterol levels, blood pressure, smoking habits and carbohydrate tolerance among the precarious and nonprecarious groups because many of these cases were studied long before the significance of risk factors was understood. However, we believe that the risk factors are probably distributed randomly through the study population because the subjects all had established coronary obstructive disease at entry into the study. The only characteristic that separated them into precarious and nonprecarious was whether obstructive lesions were incomplete or complete.

A striking feature of the survival curves in all three of the methods of analysis—number of vessels, angiographic score and precariousness—is the wide divergence of the various categories in the first five years, with survival leveling off at that point in all but the most severely diseased. The implication is that after the first five years the disease becomes less active and the chance of death decreases. The reason for this trend might be that once coronary stenotic lesions become narrow enough to cause myocardial ischemia and thereby make the disease symptomatically evident, closure is likely to occur within five years, producing a coronary event if closure is abrupt but allowing collateral adaptation if closure proceeds gradually. Once the adaptation has been attained, an inherently stable nonprecarious state may permit long-term survival. The previously precarious state tends to evolve into a state of clinical stability.

Suggestive evidence that progression from the incomplete threatening lesion to the completely closed collateralized lesion was found when we studied the sequential angiograms of the 25 patients in our study in whom two coronary angiograms were done at least one year apart. The findings are listed in Table 2. Over three to four years, 60 percent of the stenotic lesions became narrower (32 of 53). Twelve of these 32 lesions went to complete closure but only two of them produced myocardial infarction. The other ten closed without producing a coronary event. Most of the closures, therefore, were associated with physiologic adaptations that changed a high-risk state to a low-risk state, from precarious to nonprecarious.

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